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=> s HCV and "E2" and antibody and DNA
         11988 HCV
            27 HCVS
         11992 HCV
                 (HCV OR HCVS)
         31490 "E2"
        398512 ANTIBODY
        412957 ANTIBODIES
        614922 ANTIBODY
                 (ANTIBODY OR ANTIBODIES)
        661737 DNA
         11362 DNAS
        663115 DNA
                 (DNA OR DNAS)
L1          79 HCV AND "E2" AND ANTIBODY AND DNA

=> display l1
ENTER ANSWER NUMBER OR RANGE (1):60-79
ENTER DISPLAY FORMAT (BIB):bib abs

L1   ANSWER 60 OF 79     MEDLINE
AN   97140461     MEDLINE
DN   97140461   PubMed ID: 8986942
TI   Antibody responses to the hepatitis C virus E2
     protein: relationship to viraemia and prevalence in anti-HCV
     seronegative subjects.
AU   Cerino A; Bissolati M; Cividini A; Nicosia A; Esumi M; Hayashi N; Mizuno
     K; Slobbe R; Oudshoorn P; Silini E; Asti M; Mondelli M U
CS   Istituto di Clinica delle Malattie Infettive, Pavia, Italy.
SO   JOURNAL OF MEDICAL VIROLOGY, (1997 Jan) 51 (1) 1-5.
     Journal code: 7705876. ISSN: 0146-6615.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   199703
ED   Entered STN: 19970414
     Last Updated on STN: 19990129
     Entered Medline: 19970328
AB   A small proportion of patients with chronic hepatitis C virus (HCV
     ) infection show no serological responses to the HCV
     polypeptides incorporated in commercial III generation immunoassays. To
     determine whether sera from these subjects contain antibodies to
     the highly immunoreactive second envelope polypeptide E2, which
     is not included in current anti-HCV assays, we studied 59 anti-
```

HCV negative subjects who were found consistently to be **HCV** RNA positive by polymerase chain reaction (PCR). Controls included 167 anti-**HCV** seropositive patients with or without serum **HCV** RNA and normal subjects. **Antibodies** to the **E2** region were sought for by ELISA using the following antigens: a full length **E2** protein expressed in insect cells using a baculovirus vector and extracted under denaturing conditions (dE2), and a C-terminal truncated soluble **E2** (sE2) protein (a.a. 390-683), also expressed with a baculovirus vector, containing a signal peptide of rabies virus G protein which allows its secretion into the culture supernatant. Sera from only two (3.4%) of the 59 anti-**HCV** negative, **HCV** RNA positive patients recognised sE2 and none dE2. In sharp contrast, 82% of seropositive, viraemic patients recognised sE2 and 60% dE2, the difference in immunoreactivity being statistically significant ($P < 0.0003$). A significantly lower proportion of sera from anti-**HCV** positive, **HCV** RNA negative subjects recognised either sE2 or dE2 (16% and 13%, respectively, $P < 0.000001$). Healthy controls were consistently negative. These results indicate that **antibody** responses to predominantly conformational epitopes on the **HCV E2** protein are common in patients with chronic **HCV** infection and are strictly related to the presence of circulating viral genomes. In contrast, only a minor proportion of **HCV** RNA positive patients, but anti-**HCV** seronegative by commercial immunoassays, have humoral immune responses to the **HCV E2** region.

L1 ANSWER 61 OF 79 MEDLINE
AN 97118791 MEDLINE
DN 97118791 PubMed ID: 8959633
TI Significance of anti-**E2** in the diagnosis of **HCV** infection in patients on maintenance hemodialysis: anti-**E2** is frequently detected among anti-**HCV** **antibody**-negative patients.
AU Lee D S; Lesniewski R R; Sung Y C; Min W K; Park S G; Lee K H; Kim H S
CS Department of Clinical Pathology, Korea Cancer Center Hospital, Seoul.
SO JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY, (1996 Nov) 7 (11) 2409-13. Journal code: 9013836. ISSN: 1046-6673.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199703
ED Entered STN: 19970321
Last Updated on STN: 19980206
Entered Medline: 19970313
AB A routine screening test used in the diagnosis of hepatitis C virus (**HCV**) infection is the anti-**HCV** **antibody** (anti-**HCV**) test containing core, NS3, NS4, and NS5 antigens of **HCV**. When **HCV** infection occurs in immunocompromised hosts, **antibody** formation against core, NS3, or NS4 antigens may be weak in the presence of **HCV** viremia and cannot be detected by routine anti-**HCV** tests. This study proposed that in immunocompromised hosts such as patients with chronic renal failure (whose capacity to form **antibodies** is diminished), **antibody** formation against the **E2** region would be preserved, because the **E2**/NS1 region of **HCV** is strongly immunogenic. The aim of this study is to evaluate the significance of anti-**E2** in the diagnosis of **HCV** infection among patients on maintenance hemodialysis who are anti-**HCV**-negative, using a conventional third-generation enzyme immunoassay (EIA) kit. The **E2**/NS1 gene of **HCV** encoding the amino acid sequence.388-664 was molecularly cloned into a vector containing an SV 40 promotor and was expressed in Chinese Hamster ovary cells. Using this **E2** protein, the anti-**E2** test was performed by EIA on 100 patients on maintenance

hemodialysis, and on 50 patients with chronic hepatitis C who were anti-**HCV**-positive, to evaluate the antigenecity of the **E2** protein. Of the 100 hemodialysis patients, 15 (15.0%) tested anti-**HCV**-positive using a third generation anti-**HCV** ELISA kit. Of the 85 patients who tested negative for anti-**HCV**, nine (10.6%) were anti-**E2**-positive and six (66.7%) of these anti-**E2** positive patients showed **HCV** RNA viremia by **HCV** reverse transcription-polymerase chain reaction. Fourty-two (84.0%) of 50 patients with chronic hepatitis C were anti-**E2** -positive. As a control group, we tested for anti-**E2** among 30 blood donors who were anti-**HCV**-negative, and also among 85 patients with hepatocellular carcinoma who were anti-**HCV** -negative, but in both groups, none (0%) was anti-**E2**-positive. In conclusion, these data suggest that the **E2** protein of **HCV** should be included in a diagnostic anti-**HCV** kit for the detection of **HCV** infection in immunocompromised patients.

L1 ANSWER 62 OF 79 MEDLINE
AN 97092739 MEDLINE
DN 97092739 PubMed ID: 8938159
TI Hypervariable region sequence in cryoglobulin-associated hepatitis C virus in sera of patients with chronic hepatitis C: relationship to **antibody** response against hypervariable region genome.
CM Comment in: Hepatology. 1999 Feb;29(2):614-5
AU Aiyama T; Yoshioka K; Okumura A; Takayanagi M; Iwata K; Ishikawa T; Kakumu S
CS Third Department of Internal Medicine, Nagoya University School of Medicine, Japan.
SO HEPATOLOGY, (1996 Dec) 24 (6) 1346-50.
Journal code: 8302946. ISSN: 0270-9139.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199701
ED Entered STN: 19970128
Last Updated on STN: 20000303
Entered Medline: 19970109
AB Essential mixed cryoglobulinemia is frequently associated with hepatitis C virus (**HCV**) infection, with the formation of **HCV** antigen/**antibody** complexes. The hypervariable region (HVR) of the **HCV E2**/NS1 region is thought to include epitopes for neutralizing **antibodies**, but it remains uncertain whether cryoglobulins (CGs) contain such **antibody**-bound **HCV**. Thus, we studied HVR clones isolated from cryoprecipitate and supernatant in the sera of four chronic hepatitis C patients with cryoglobulinemia, and expressed as fusion proteins with glutathione S-transferase (GST). Patients' sera were tested for **antibody** binding to the proteins. The rate of anti-HVR **antibody**-positive clones was significantly higher in cryoprecipitate (89% +/- 13%, P < .05) than in supernatant (41% +/- 25%). Both **HCV** RNA and anti-HVR **antibody** were more concentrated in cryoprecipitates compared with those of serum and supernatant in two patients tested. Anti-HVR **antibody**-positive clones in cryoprecipitate showed common amino acid (aa) sequences in each of the four patients. Similarly, all the **antibody**-positive clones in supernatant showed the same aa sequences for three of the four patients. When aa sequences were compared with those of reported isolates with genotype 1b, the mean percentage of aa difference was greater in the clones from supernatant and in anti-HVR **antibody**-negative clones than in the clones from cryoprecipitate and in the **antibody** -positive clones, respectively. These findings indicate that serum CG contains anti-HVR **antibody**-bound **HCV** in patients with chronic hepatitis C. Anti-HVR **antibody**-free individual clones, which were more frequently noted in supernatant, showed closely related

sequences, but which were of a heterogeneous quasispecies nature.

L1 ANSWER 63 OF 79 MEDLINE
AN 97051514 MEDLINE
DN 97051514 PubMed ID: 8896240
TI Purification and in vitro-phospholabeling of secretory envelope proteins E1 and **E2** of hepatitis C virus expressed in insect cells.
AU Hussy P; Schmid G; Mous J; Jacobsen H
CS Department of a Pharmaceutical Research-Gene Technology, Basel, Switzerland.. Peter.Huessy@Roche.com
SO VIRUS RESEARCH, (1996 Nov) 45 (1) 45-57.
Journal code: 8410979. ISSN: 0168-1702.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199704
ED Entered STN: 19970414
Last Updated on STN: 19970414
Entered Medline: 19970403
AB The putative envelope glycoproteins of hepatitis C virus (**HCV**), E1 and **E2**, were expressed as recombinant, secretory proteins in Sf9 insect cells through infection with recombinant baculoviruses. The influenza virus hemagglutinin signal sequence (HASS) was inserted upstream of the **HCV**-cDNAs in order to effect secretion. Furthermore, a hexa-histidine tag for purification on a Ni(2+)-nitrilotriacetic acid (Ni(2+)-NTA) column and a protein kinase A (PKA) recognition sequence for in vitro-phospholabeling were fused upstream of the **HCV**-cDNA. E1- and **E2** proteins lacking their carboxy-terminal, hydrophobic sequence were produced by baculovirus-infected insect cells in bioreactors of 23 1. The medium was concentrated and proteins were purified under native conditions on Ni(2+)-NTA columns. Purified proteins could be phospholabeled in vitro using the catalytic subunit of protein kinase. A isolated from bovine heart and gamma-[32P]ATP. Labeled E1 and **E2** proteins expressed in insect cells could be immunoprecipitated with sera from **HCV**-infected patients. Co-expression of these E1 and **E2** proteins led to the formation of E1-**E2** complexes within the insect cell and to secretion of these complexes into the medium.

L1 ANSWER 64 OF 79 MEDLINE
AN 97021254 MEDLINE
DN 97021254 PubMed ID: 8867614
TI Murine humoral immune response against recombinant structural proteins of hepatitis C virus distinct from those of patients.
AU Ahmed M; Shikata T; Esumi M
CS First Department of Pathology, Nihon University School of Medicine, Tokyo, Japan.
SO MICROBIOLOGY AND IMMUNOLOGY, (1996) 40 (2) 169-76.
Journal code: 7703966. ISSN: 0385-5600.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961205
AB We examined the humoral immune response to recombinant structural proteins of hepatitis C virus (**HCV**) such as C, E1 and **E2** in immunized mice. Mice showed high induction of **antibodies** against these three structural proteins. Conformational and/or linear epitopes of these regions showed high responses in mice. Comparison with patients revealed higher anti-E1 and anti-**E2** responses in mice and 15

immunoreactive peptides which are unique to mice, especially 11 peptides from the **E2** region. The hydrophilic regions of these proteins were found to be the most immunogenic. Therefore, the murine immune system against recombinant E1 and **E2** glycoproteins was distinct from those of patients in natural infection, and may be a target to find protective activity against **HCV** infection.

L1 ANSWER 65 OF 79 MEDLINE
AN 96423206 MEDLINE
DN 96423206 PubMed ID: 8825807
TI Hepatitis C viral infection in thalassemic children: clinical and molecular studies.
AU Ni Y H; Chang M H; Lin K H; Chen P J; Lin D T; Hsu H Y; Chen D S
CS Department of Pediatrics, National Taiwan University, Taipei.
SO PEDIATRIC RESEARCH, (1996 Feb) 39 (2) 323-8.
Journal code: 0100714. ISSN: 0031-3998.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199612
ED Entered STN: 19970128
Last Updated on STN: 19970128
Entered Medline: 19961203
AB To determine and correlate the liver function profile, hepatitis C virus (**HCV**) genome, anti-**HCV**, genotypes, quantitation, and nucleotide sequence variability in polytransfused thalassemic children, 61 such children were studied prospectively for 4 y. Twenty-six had **HCV** infection. The average age, number of transfusions, and alanine aminotransferase (ALT) levels of the **HCV**-infected group were higher than those of the 35 children without **HCV** infection. None was infected after the initiation of anti-**HCV** screening in donor blood. Liver biopsies were performed in six **HCV**-infected and eight **HCV**-noninfected thalassemic children, and portal fibrosis was found more frequently in the **HCV**-infected group. Quantitation of **HCV** RNA was done by the competitive polymerase chain reaction method, and the titer was about 1 x 10(6) to 5 x 10(8) copies/mL. The titer did not change significantly over the 4-y follow-up period and did not correlate with ALT levels. Nineteen **HCV** -infected patients were genotyped; 15 were Okamoto/Simmonds type II/1b, two were type III/2a, and two were type IV/2b. The hypervariable region of the **HCV** genome (**E2**/NS1) was cloned and sequenced in two serum samples from one patient collected at a 2-y interval, as the ALT levels decreased. The variation rate was estimated to be 1.2-1.7 x 10(-2)/nucleotide/y. The results showed that, in polytransfused thalassemic children, 43% (26/61) contracted **HCV**. We conclude that **HCV** infection may cause elevated ALT levels and portal fibrosis of the liver, whereas the viral titer and genotypes do not parallel ALT levels.

L1 ANSWER 66 OF 79 MEDLINE
AN 96105330 MEDLINE
DN 96105330 PubMed ID: 7503672
TI The serology of hepatitis C virus (**HCV**) infection: **antibody** crossreaction in the hypervariable region 1.
AU da Silva Cardoso M; Siemoneit K; Nemecek V; Epple S; Koerner K; Kubanek B
CS German Red Cross, Ulm, Federal Republic of Germany.
SO ARCHIVES OF VIROLOGY, (1995) 140 (10) 1705-13.
Journal code: 7506870. ISSN: 0304-8608.
CY Austria
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-X81467; GENBANK-X81468; GENBANK-X81469; GENBANK-X81470;

GENBANK-X81471
EM 199601
ED Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960116
AB We determined the NS1/**E2** N-terminal sequence including the hypervariable region 1 (HVR1) from five individuals chronically infected with **HCV**: two from the Czech Republic and three from Germany. From each sequence, six 12-mer overlapping peptides were synthesized and used in a peptide scan to evaluate seroreactivity of each of those patients, as well as three anti-**HCV** positive blood donors to the different isolates. We could show the general presence of **antibodies** to multiple HVR1 specific sequences reflecting the existence of multiple variants in infected persons. Finally, we observed the persistance of **HCV** infections in all individuals despite an active humoral response directed against the virus.

L1 ANSWER 67 OF 79 MEDLINE
AN 96061548 MEDLINE
DN 96061548 PubMed ID: 7595420
TI Fraction-specific populations of the hypervariable region of the hepatitis C virus in a patient with cryoglobulinemia.
AU Kurosaki M; Enomoto N; Nouchi T; Sakuma I; Marumo F; Sato C
CS Second Department of Internal Medicine, Faculty of Medicine, Tokyo Medical and Dental University, Japan.
SO JOURNAL OF MEDICAL VIROLOGY, (1995 Aug) 46 (4) 403-8.
Journal code: 7705876. ISSN: 0146-6615.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199511
ED Entered STN: 19960124
Last Updated on STN: 19960124
Entered Medline: 19951128
AB Nucleotide sequences of the hypervariable region (HVR) of the **E2** /NS1 gene of hepatitis C virus (**HCV**), which are now thought to contain epitopes for neutralizing **antibodies**, were compared between **antibody**-bound **HCV** and free **HCV** in a patient with type II cryoglobulinemia. **Antibody**-bound **HCV** was immunoprecipitated with anti-human immunoglobulins from serum of the patient. Total RNA was recovered from the pellet and the supernatant, respectively, and the envelope gene containing the HVR was amplified by the reverse transcription and nested polymerase chain reaction. The amplified cDNA was examined by the single strand conformation polymorphism (SSCP) analysis. Sequences of bands separated by SSCP analysis were determined by the dideoxy chain termination method. SSCP analyses revealed that the **HCV** populations were completely different between **antibody**-bound **HCV** and free **HCV**: **antibody**-bound **HCV** was composed of two bands and free **HCV** was composed of three bands. These five bands showed different mobility with each other on the SSCP gel. Sequencing of each band revealed distinct HVR sequences, differing in 1-34 nucleotides and 1-15 deduced amino acids. Three sequences of free **HCV** was similar with each other (1-5 nucleotide and 1-4 amino acid differences). On the other hand, two sequences of **antibody**-bound **HCV** had 5-34 nucleotide and 5-15 amino acid differences with free **HCV** . Thirteen amino acids in the 5' of HVR were completely identical in three sequences of free **HCV**, whereas there were three and seven amino acid differences in two sequences of **antibody**-bound **HCV** . These findings suggest that isolated specific epitopes for envelope **antibodies** exist within the HVR.(ABSTRACT TRUNCATED AT 250 WORDS)

L1 ANSWER 68 OF 79 MEDLINE

AN 95266271 MEDLINE
DN 95266271 PubMed ID: 7538251
TI **Antibodies** in human sera specific to hypervariable region 1 of hepatitis C virus can block viral attachment.
AU Zibert A; Schreier E; Roggendorf M
CS Institute of Virology, University of Essen, Germany.
SO VIROLOGY, (1995 Apr 20) 208 (2) 653-61.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199506
ED Entered STN: 19950621
Last Updated on STN: 19960129
Entered Medline: 19950609
AB It has been postulated that **antibodies** specific to the hypervariable region 1 (HVR1) within the putative envelop protein **E2** of hepatitis C virus (**HCV**) can neutralize virus. We studied such **antibodies** in sera of patients who were infected in a single-source outbreak by a contaminated anti-D immunoglobulin preparation (**HCV**-AD78). The nucleotide sequences of cDNAs encoding HVR1 of **HCV**-AD78 were determined. The four major variants (HVR1.A, B, C, and D) were expressed as fusion proteins in Escherichia coli. Sixty-seven percent of sera contained **antibodies** to HVR1.A. Sera unrelated to infection of the outbreak also recognized HVR1.A but to a lesser extent (15%), suggesting that not all HVR1-specific **antibodies** are absolutely isolate-specific. **Antibodies** directed against individual variants of HVR1 were found in sera obtained early postinfection (p.i.) (< or = 1 year) but also in sera obtained several years later. An in vitro binding assay of **HCV** to tissue culture cells was employed to further characterize these sera. Five of seven sera that were obtained early p.i. prevented binding of **HCV** to cells. Preincubation of such sera with HVR1-specific fusion proteins restored binding of **HCV** to cells in four of five sera. These findings suggest that the majority of neutralizing **antibodies** are directed against HVR1.

L1 ANSWER 69 OF 79 MEDLINE
AN 95146514 MEDLINE
DN 95146514 PubMed ID: 7844127
TI Transmission of the hepatitis-C virus by tissue transplantation.
AU Conrad E U; Gretch D R; Obermeyer K R; Moogk M S; Sayers M; Wilson J J; Strong D M
CS Northwest Tissue Center/Puget Sound Blood Center, Seattle, Washington.
SO JOURNAL OF BONE AND JOINT SURGERY. AMERICAN VOLUME, (1995 Feb) 77 (2) 214-24.
Journal code: 0014030. ISSN: 0021-9355.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; AIDS
EM 199503
ED Entered STN: 19950316
Last Updated on STN: 19950316
Entered Medline: 19950307
AB The hepatitis-C virus has been the most prevalent cause of chronic hepatitis in both blood and organ recipients. The introduction of a second-generation immunoassay for **antibodies** to the hepatitis-C virus (**HCV** 2.0) provided the opportunity to determine if the hepatitis-C virus can be transmitted through tissue transplantation. Banked sera from tissue donors that had previously been found to be non-reactive to the first-generation hepatitis-C virus **antibody** assay (**HCV** 1.0) and non-reactive for **antibodies** to

hepatitis-B core antigen were retested with **HCV** 2.0. The sera from two donors were reactive; the transplant records of recipients of tissues from these donors were reviewed, and the surgeons or hospitals were contacted. The tissue recipients were tested with **HCV** 2.0, and positive sera were tested for hepatitis-C virus RNA by polymerase chain reaction. Viral nucleic acids isolated from viremic donors and recipients were analyzed for identity by sequencing of the hepatitis-C virus envelope gene (**E2**) hypervariable region. There were twenty-one grafts, which had been treated with gamma radiation, from one donor; thirteen had been transplanted to twelve recipients. Serum samples from six of the recipients were tested; one was reactive. This patient had other risk factors for infection with the hepatitis-C virus, and sequence analysis demonstrated non-identity between the donor and recipient hepatitis-C virus isolates. Nine of twelve grafts from a second donor had been transplanted in nine recipients. Serum samples from five patients were tested with **HCV** 2.0; four were reactive. In three of the four patients, the sera were determined to be positive for the hepatitis-C virus by polymerase chain reaction. **E2** sequence analyses of hepatitis-C virus RNA isolates from two of these recipients demonstrated sequence identity with the donor isolate. The results of the present report demonstrate that the hepatitis-C virus can be transmitted by bone, ligament, and tendon allografts. They also support the need for testing of all tissue donors for **antibodies** to the hepatitis-C virus before the tissue is released for transplantation. The results also suggest that seventeen kilo-gray of gamma radiation may inactivate the hepatitis-C virus in tissue.

L1 ANSWER 70 OF 79 MEDLINE
AN 95088611 MEDLINE
DN 95088611 PubMed ID: 7996156
TI Nucleotide sequence of hepatitis C virus (type 3b) isolated from a Japanese patient with chronic hepatitis C.
AU Chayama K; Tsubota A; Koida I; Arase Y; Saitoh S; Ikeda K; Kumada H
CS Department of Gastroenterology, Toranomon Hospital, Okinaka Memorial Institute for Medical Research, Tokyo, Japan.
SO JOURNAL OF GENERAL VIROLOGY, (1994 Dec) 75 (Pt 12) 3623-8.
Journal code: 0077340. ISSN: 0022-1317.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-D10585; GENBANK-D11443; GENBANK-D49374
EM 199501
ED Entered STN: 19950126
Last Updated on STN: 19960129
Entered Medline: 19950113
AB The genomic sequences of many hepatitis C virus (**HCV**) isolates have been reported and a variety of virus genotypes have been classified based on homology in the conserved regions. We have previously identified five distinct genotypes (1a, 1b, 2a, 2b and 3b) in Japanese patients with chronic **HCV** infection by comparing the sequences of the NS5 region. The complete nucleotide sequence for five genotypes (1a, 1b, 1c, 2a and 2b) have already been reported and we report here the complete nucleotide sequence of genotype 3b. The isolate (**HCV** Tr) was 9439 nucleotides long, excluding the poly(U) tract at its 3' end, and encodes a single long open reading frame of 3023 amino acids. Total nucleotide sequence homologies were 68.4 to 68.7%, 68.3 to 69.0%, 67.2%, 65.8% and 65.6% compared with type 1a, 1b, 1c, 2a and 2b genomes, respectively. The amino acid sequences of these five genotypes were highly homologous in the core, NS3 and NS5B regions, but the **E2**/NS1 region, which contains hypervariable regions 1 and 2, and the NS5A region were poorly conserved. Although it was possible to detect **antibody** against the relatively homologous core and NS3 regions by ELISA, the presence of divergent protein structures must be taken into account in the

development of a vaccine.

L1 ANSWER 71 OF 79 MEDLINE
AN 95088441 MEDLINE
DN 95088441 PubMed ID: 7527827
TI Confirmation of hepatitis C virus transmission through needlestick accidents by molecular evolutionary analysis.
AU Suzuki K; Mizokami M; Lau J Y; Mizoguchi N; Kato K; Mizuno Y; Sodeyama T; Kiyosawa K; Gojobori T
CS Second Department of Medicine, Nagoya City University Medical School.
SO JOURNAL OF INFECTIOUS DISEASES, (1994 Dec) 170 (6) 1575-8.
Journal code: 0413675. ISSN: 0022-1899.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 199501
ED Entered STN: 19950126
Last Updated on STN: 19960129
Entered Medline: 19950113
AB To document the transmission of hepatitis C virus (**HCV**) through needlestick accidents, 3 health workers who acquired **HCV** through such accidents and their **HCV** donor patients were studied using molecular evolutionary analysis based on the **HCV E2** region. At least six clones were sequenced from each subject. Nucleotide substitutions were estimated by the six-parameter method, and a phylogenetic tree was constructed by the neighbor-joining method. **HCV** isolates from the donor patient and the recipient were nested in one monophyletic cluster; this clustering was confirmed to be statistically significant by bootstrap analysis. The nucleotide divergence among the isolates from the recipient was always smaller than that from the donor, supporting the notion that the direction of transmission was from the donor to the recipient. These findings provide evidence, at a molecular evolutionary level, that **HCV** was transmitted through needlestick accidents.

L1 ANSWER 72 OF 79 MEDLINE
AN 94365917 MEDLINE
DN 94365917 PubMed ID: 8083956
TI Formation and intracellular localization of hepatitis C virus envelope glycoprotein complexes expressed by recombinant vaccinia and Sindbis viruses.
AU Dubuisson J; Hsu H H; Cheung R C; Greenberg H B; Russell D G; Rice C M
CS Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, Missouri 63110-1093.
NC CA57973 (NCI)
F05TW04765 (FIC)
SO JOURNAL OF VIROLOGY, (1994 Oct) 68 (10) 6147-60.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199410
ED Entered STN: 19941021
Last Updated on STN: 19941021
Entered Medline: 19941013
AB Hepatitis C virus (**HCV**) encodes two putative virion glycoproteins (E1 and **E2**) which are released from the polyprotein by signal peptidase cleavage. In this report, we have characterized the complexes formed between E1 and **E2** (called E1E2) for two different **HCV** strains (H and BK) and studied their intracellular localization. Vaccinia virus and Sindbis virus vectors were used to express the **HCV** structural proteins in three different

cell lines (HepG2, BHK-21, and PK-15). The kinetics of association between E1 and **E2**, as studied by pulse-chase analysis and coprecipitation of **E2** with an anti-E1 monoclonal **antibody**, indicated that formation of stable E1E2 complexes is slow. The times required for half-maximal association between E1 and **E2** were 60 to 85 min for the H strain and more than 165 min for the BK strain. In the presence of nonionic detergents, two forms of E1E2 complexes were detected. The predominant form was a heterodimer of E1 and **E2** stabilized by noncovalent interactions. A minor fraction consisted of heterogeneous disulfide-linked aggregates, which most likely represent misfolded complexes. Posttranslational processing and localization of the **HCV** glycoproteins were examined by acquisition of endoglycosidase H resistance, subcellular fractionation, immunofluorescence, cell surface immunostaining, and immunoelectron microscopy. **HCV** glycoproteins containing complex N-linked glycans were not observed, and the proteins were not detected at the cell surface. Rather, the proteins localized predominantly to the endoplasmic reticular network, suggesting that some mechanism exists for their retention in this compartment.

L1 ANSWER 73 OF 79 MEDLINE
AN 94360003 MEDLINE
DN 94360003 PubMed ID: 8078948
TI The physical state of the negative strand of hepatitis C virus RNA in serum of patients with chronic hepatitis C.
AU Shindo M; Di Bisceglie A M; Akatsuka T; Fong T L; Scaglione L; Donets M; Hoofnagle J H; Feinstone S M
CS Liver Diseases Section, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD 20892.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1994 Aug 30) 91 (18) 8719-23.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199410
ED Entered STN: 19941013
Last Updated on STN: 19941013
Entered Medline: 19941004
AB Negative strands of the hepatitis C virus (**HCV**) genome (a positive-stranded RNA virus) have been found in a nuclease-resistant form in the serum of patients with **HCV** infections. We determined whether a complete negative-strand copy is present in the serum, whether the negative strand is particle-associated, and finally, whether it is virion-associated and encapsidated like the positive (genomic) strand. Isopyknic sucrose and cesium chloride density ultracentrifugation followed by a strand-specific reverse transcription-polymerase chain reaction on the collected fractions was performed to determine whether both positive and negative strands were associated with similar particles. Both strands comigrated to approximately the same density (1.11-1.16 g/cm3) in sucrose. After treatment of the plasma with detergent (0.1% Nonidet P-40) to remove the viral envelope and centrifugation on cesium chloride gradients, the positive strands shifted to a density of 1.35 g/cm3, and the negative strands were not detected. By using **antibodies** specific for the **HCV** core or envelope glycoproteins E1 or **E2** coated onto the wells of a microtiter plate, it was possible to specifically bind **HCV** or viral cores to the solid phase. Pelleted virus particles were resuspended in either PBS or PBS with 0.1% Nonidet P-40 to expose the core. These pellets were then incubated in **antibody**-coated microtiter wells. RNA extracted from the bound and unbound fractions was tested for **HCV** RNA. The anti-core **antibody** was able to bind positive strands but not negative strands only in detergent-treated samples. In the nondetergent-treated pellets, the anti-E1 and -**E2**

bound the positive strand, but only anti-E1 bound the negative strands. These findings indicate that while both strands of **HCV** RNA can be detected in serum, the positive strand is encapsidated within the enveloped core, and the negative strand appears to be in a membrane particle associated with the viral envelope protein E1 but does not appear to be within the **HCV** core of circulating virions.

L1 ANSWER 74 OF 79 MEDLINE
AN 94267419 MEDLINE
DN 94267419 PubMed ID: 8207402
TI Fluctuation of hepatitis C virus quasispecies in persistent infection and interferon treatment revealed by single-strand conformation polymorphism analysis.
AU Enomoto N; Kurosaki M; Tanaka Y; Marumo F; Sato C
CS Second Department of Internal Medicine, Faculty of Medicine, Tokyo Medical and Dental University, Japan.
SO JOURNAL OF GENERAL VIROLOGY, (1994 Jun) 75 (Pt 6) 1361-9.
Journal code: 0077340. ISSN: 0022-1317.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-S72416; GENBANK-S72417; GENBANK-S72418; GENBANK-S72433
EM 199407
ED Entered STN: 19940721
Last Updated on STN: 19960129
Entered Medline: 19940713
AB Hepatitis C virus (**HCV**) populations in vivo consist of heterogeneous mixtures of genetically different but closely related variants defined as a 'quasispecies'. The longitudinal fluctuation of **HCV** quasispecies populations in chronic hepatitis C has not been elucidated. Serial plasma samples were obtained from four patients with chronic hepatitis C (two patients without any treatment and two patients treated with interferon), and cDNA fragments containing the 5'-terminal region of the **E2** gene of **HCV** were amplified from plasma RNA using PCR. Since conventional cloning of PCR products detects only a small part of the entire population, PCR products of each sample were separated by electrophoresis using single-strand conformation polymorphism (SSCP) analysis, which can distinguish **DNA** fragments of the same size as different electrophoretic bands depending on their sequence-specific conformation. Separated **DNA** fragments were recovered from SSCP bands in gels and their nucleotide sequences determined. SSCP electrophoresis separated PCR products into bands with different mobility. Sequence analysis of these bands confirmed that **HCV** populations in each patient are composed of quasispecies with different **E2**-hypervariable regions (HVR), which are known to contain **antibody** epitopes. Different patterns of variation in the HVR of quasispecies were observed in individual patients with different clinical features over time during chronic infection. Following interferon treatment, some quasispecies disappeared during the treatment and reappeared after the end of the treatment, whereas other quasispecies in the same patient remained during the treatment suggesting that the sensitivity to interferon is different among quasispecies.

L1 ANSWER 75 OF 79 MEDLINE
AN 94141472 MEDLINE
DN 94141472 PubMed ID: 7508488
TI Sequential change of the hypervariable region of the hepatitis C virus genome in acute infection.
AU Sakamoto N; Enomoto N; Kurosaki M; Marumo F; Sato C
CS Second Department of Internal Medicine, Faculty of Medicine, Tokyo Medical and Dental University, Japan.
SO JOURNAL OF MEDICAL VIROLOGY, (1994 Jan) 42 (1) 103-8.
Journal code: 7705876. ISSN: 0146-6615.

CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199403
ED Entered STN: 19940330
Last Updated on STN: 19980206
Entered Medline: 19940315
AB Hepatitis C virus (**HCV**) infection is characterized by persistence of liver inflammation that often leads to end-stage liver disease, although the mechanisms are not fully understood. A hypervariable region (HVR) has been reported in the **E2**/NS1 region of the **HCV** genome, in which striking diversity is found among different **HCV** isolates. To investigate the association of the HVR alterations with the clinical courses of **HCV** infection, a longitudinal analysis of the HVR in patients with acute **HCV** infection was carried out. Plasma samples were obtained at several times in three patients with acute hepatitis C. Plasma RNA was extracted and reverse transcribed, and **DNA** fragments that included the HVR were amplified by PCR. The sequences of the HVR were directly determined from the PCR products by the dideoxy chain termination method, from which amino acid sequences were deduced. In all cases, plasma **HCV**-RNA disappeared with the improvement of the initial alanine aminotransferase (ALT) elevation, but **HCV**-RNA reappeared about 1 year later with or without deterioration of the hepatitis. In a case of sporadic acute hepatitis, the **HCV** in the recurrent phase had seven amino acid substitutions in the HVR compared with that in the acute phase, although no amino acid changes were noted during the initial acute phase. In a case of posttransfusion hepatitis, a marked difference was observed between the acute and the recurrent phases, with an amino acid homology of 30% (8/27). The mutation rate of the HVR had a tendency to accelerate as the **HCV** infection progressed to the chronic stage.(ABSTRACT TRUNCATED AT 250 WORDS)

L1 ANSWER 76 OF 79 MEDLINE
AN 93218090 MEDLINE
DN 93218090 PubMed ID: 7681882
TI Expression of hepatitis C virus genome.
AU Nishihara T; Mizuno K; Shikata T
CS First Department of Pathology, Nihon University School of Medicine.
SO NIPPON RINSHO. JAPANESE JOURNAL OF CLINICAL MEDICINE, (1993 Feb) 51 (2) 323-8. Ref: 17
Journal code: 0420546. ISSN: 0047-1852.
CY Japan
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA Japanese
FS Priority Journals
EM 199304
ED Entered STN: 19930521
Last Updated on STN: 19970203
Entered Medline: 19930430
AB Complementary **DNAs** from **HCV** genome were expressed and analyzed. C8-2 protein, a part of NS5, and core protein were synthesized in E. coli. Core protein (JCC) was appeared to be very useful for diagnostic probe of **HCV** infection. Predicted envelope glycoproteins (E1 and **E2**/NS1) produced in infected insect cells were glycosylated and secreted into the culture media when the signal sequence of rabies virus G protein was introduced. An ELISA was developed using each purified recombinant protein. Anti-E1 **antibody** was detected in 20% of patients with non-A, non-B chronic liver diseases, whereas anti-**E2**/NS1 **antibody** was detected in more than 88%. These results indicate that the immune responses against these

glycoproteins are different.

L1 ANSWER 77 OF 79 MEDLINE
AN 93172357 MEDLINE
DN 93172357 PubMed ID: 7679746
TI Expression and identification of hepatitis C virus polyprotein cleavage products.
AU Grakoui A; Wychowski C; Lin C; Feinstone S M; Rice C M
CS Department of Molecular Microbiology, Washington University School of Medicine, St. Louis, Missouri 63110-1093.
NC CA57973 (NCI)
SO JOURNAL OF VIROLOGY, (1993 Mar) 67 (3) 1385-95.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199303
ED Entered STN: 19930402
Last Updated on STN: 19970203
Entered Medline: 19930323
AB Hepatitis C virus (**HCV**) is the major cause of transfusion-acquired non-A, non-B hepatitis. **HCV** is an enveloped positive-sense RNA virus which has been classified as a new genus in the flavivirus family. Like the other two genera in this family, the flaviviruses and the pestiviruses, **HCV** polypeptides appear to be produced by translation of a long open reading frame and subsequent proteolytic processing of this polyprotein. In this study, a cDNA clone encompassing the long open reading frame of the **HCV** H strain (3,011 amino acid residues) has been assembled and sequenced. This clone and various truncated derivatives were used in vaccinia virus transient-expression assays to map **HCV**-encoded polypeptides and to study **HCV** polyprotein processing. **HCV** polyproteins and cleavage products were identified by using convalescent human sera and a panel of region-specific polyclonal rabbit antisera. Similar results were obtained for several mammalian cell lines examined, including the human HepG2 hepatoma line. The data indicate that at least nine polypeptides are produced by cleavage of the **HCV** H strain polyprotein. Putative structural proteins, located in the N-terminal one-fourth of the polyprotein, include the capsid protein C (21 kDa) followed by two possible virion envelope proteins, E1 (31 kDa) and **E2** (70 kDa), which are heavily modified by N-linked glycosylation. The remainder of the polyprotein probably encodes nonstructural proteins including NS2 (23 kDa), NS3 (70 kDa), NS4A (8 kDa), NS4B (27 kDa), NS5A (58 kDa), and NS5B (68 kDa). An 82- to 88-kDa glycoprotein which reacted with both **E2** and NS2-specific **HCV** antisera was also identified (called **E2**-NS2). Preliminary results suggest that a fraction of E1 is associated with **E2** and **E2**-NS2 via disulfide linkages.

L1 ANSWER 78 OF 79 MEDLINE
AN 92230232 MEDLINE
DN 92230232 PubMed ID: 1314459
TI Full-length sequence of a hepatitis C virus genome having poor homology to reported isolates: comparative study of four distinct genotypes.
AU Okamoto H; Kurai K; Okada S; Yamamoto K; Lizuka H; Tanaka T; Fukuda S; Tsuda F; Mishiro S
CS Immunology Division, Jichi Medical School, Tochigi-ken, Japan.
SO VIROLOGY, (1992 May) 188 (1) 331-41.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

OS GENBANK-D00828; GENBANK-D01221; GENBANK-D10074; GENBANK-D10075; GENBANK-D10076; GENBANK-D10077
EM 199205
ED Entered STN: 19920607
Last Updated on STN: 19970203
Entered Medline: 19920515
AB Variable genomic sequences have been reported for RNA cloned from hepatitis C virus (**HCV**)-infected humans and chimpanzees. We found that four distinct genotypes of **HCV** could be differentially identified by PCR using type-specific primers. Full-length sequences have so far been reported for three of the four **HCV** genotypes, and we report herewith the sequence of the fourth type obtained from a Japanese blood donor. The entire nucleotide sequence of the **HCV** isolate (HC-J8) comprised 9481 bases plus a 3'-terminal poly(U) stretch of variable length. Like all previous isolates, the RNA contained a single, long open reading frame for a polyprotein of 3033 amino acids. HC-J8 differed from previously reported **HCV** isolates by 23.1-33.1% in nucleotide sequence and 15.9-28.8% in amino acid sequence. Based on genomic sequence homologies, a proposed phylogenetic tree of **HCV**, with a fourth branch represented by HC-J8, allowed a classification of all **HCV** isolates whose complete or partial sequences are now known. This classification suggests that all or most **HCV** genome sequences will fall into one of the proposed four types. The classification may be helpful in designing vaccine studies and for serological investigations of possible group- and type-specific **antibodies**.

L1 ANSWER 79 OF 79 MEDLINE
AN 92228807 MEDLINE
DN 92228807 PubMed ID: 1314389
TI Evidence for immune selection of hepatitis C virus (**HCV**) putative envelope glycoprotein variants: potential role in chronic **HCV** infections.
AU Weiner A J; Geysen H M; Christopherson C; Hall J E; Mason T J; Saracco G; Bonino F; Crawford K; Marion C D; Crawford K A; +
CS Chiron Corporation, Emeryville, CA 94608.
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1992 Apr 15) 89 (8) 3468-72.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199205
ED Entered STN: 19920607
Last Updated on STN: 19970203
Entered Medline: 19920515
AB **E2**/nonstructural protein 1, the putative envelope glycoprotein (gp72) of **HCV**, possesses an N-terminal hypervariable (**E2** HV) domain from amino acids 384 to 414 of unknown significance. The high degree of amino acid sequence variation in the **E2** HV domain appears to be comparable to that observed in the human immunodeficiency virus type 1 gp120 V3 domain. This observation and the observation that the **HCV E2** HV domain lacks conserved secondary structure imply that, like the V3 loop of human immunodeficiency virus 1 gp120, the N-terminal **E2** region may encode protective epitopes that are subject to immune selection. **Antibody**-epitope binding studies revealed five isolate-specific linear epitopes located in the **E2** HV region. These results suggest that the **E2** HV domain is a target for the human immune response and that, in addition to the three major groups of **HCV**, defined by nucleotide and amino acid sequence identity among **HCV** isolates, **E2** HV-specific subgroups also exist. Analysis of the partial or complete **E2** sequences of two individuals indicated that **E2** HV

variants can either coexist simultaneously in a single individual or that a particular variant may predominate during different episodes of disease. In the latter situation, we found one individual who developed **antibodies** to a subregion of the **E2** HV domain (amino acids 396-407) specific to a variant that was predominant during one major episode of hepatitis but who lacked detectable **antibodies** to the corresponding region of a second variant that was predominant during a later episode of disease. The data suggest that the variability in the **E2** HV domain may result from immune selection. The findings of this report could impact vaccine strategies and drug therapy programs designed to control and eliminate **HCV**.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	4.76	4.97

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